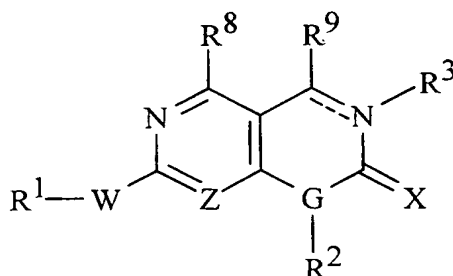


## CLAIMS

What is claimed is:

1. A compound of Formula I



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5

and the pharmaceutically acceptable salts thereof,  
wherein:

the dotted line represents an optional double bond;

Z is N or CH;

G is N or CH;

10

W is NH, S, SO, or SO<sub>2</sub>;

X is either O, S, or NR<sup>10</sup>;

$R^1, R^2$ , and  $R^{10}$  are independently selected from the group consisting of

15

H, (CH<sub>2</sub>)<sub>n</sub>Ar, COR<sup>4</sup>, (CH<sub>2</sub>)<sub>n</sub>heteroaryl, (CH<sub>2</sub>)<sub>n</sub>heterocyclyl,

C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, and C<sub>2</sub>-C<sub>10</sub>

alkynyl, wherein n is 0, 1, 2, or 3, and the  $(\text{CH}_2)_n\text{Ar}$ ,

(CH<sub>2</sub>)<sub>n</sub>heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups

are optionally substituted by up to 5 groups selected from  $\text{NR}^4\text{R}^5$ ,

N(O)R<sup>4</sup>R<sup>5</sup>, NR<sup>4</sup>R<sup>5</sup>R<sup>6</sup>Y, alkyl, phenyl, substituted phenyl,

(CH<sub>2</sub>)<sub>n</sub>heteroaryl, hydroxy, alkoxy, phenoxy, ~~thiol, thioalkyl, halo,~~

20

~~COR<sup>4</sup>, CO<sub>2</sub>R<sup>4</sup>, CONR<sup>4</sup>R<sup>5</sup>, SO<sub>2</sub>NR<sup>4</sup>R<sup>5</sup>, SO<sub>3</sub>R<sup>4</sup>, PO<sub>3</sub>R<sup>4</sup>,~~

aldehyde, nitrile, nitro,

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heteroaryloxy,  $T(\text{CH}_2)_m\text{QR}^4$ ,  $T(\text{CH}_2)_m\text{C}(\text{OR}^5)(\text{H})(\text{CH}_2)_m\text{QR}^4$ ,

$\text{C}(\text{O})\text{T}(\text{CH}_2)_m\text{QR}^4$ ,  $\text{NHC}(\text{O})\text{T}(\text{CH}_2)_m\text{QR}^4$ ,

$\text{T}(\text{CH}_2)_m\text{C}(\text{O})\text{NR}^4\text{NR}^5$ , or  $\text{T}(\text{CH}_2)_m\text{CO}_2\text{R}^4$  wherein each  $m$  is independently 1-6,  $T$  is O, S,  $\text{NR}^4$ ,  $\text{N}(\text{O})\text{R}^4$ ,  $\text{NR}^4\text{R}^6\text{Y}$ , or  $\text{CR}^4\text{R}^5$ , and  $Q$  is O, S,  $\text{NR}^5$ ,  $\text{N}(\text{O})\text{R}^5$ , or  $\text{NR}^5\text{R}^6\text{Y}$ ;

when the dotted line is present,  $\text{R}^3$  is absent;

otherwise  $\text{R}^3$  has the meanings of  $\text{R}^2$ , wherein  $\text{R}^2$  is as defined above, as well as OH,  $\text{NR}^4\text{R}^5$ ,  $\text{COOR}^4$ ,  $\text{OR}^4$ ,  $\text{CONR}^4\text{R}^5$ ,  $\text{SO}_2\text{NR}^4\text{R}^5$ ,  $\text{SO}_3\text{R}^4$ ,  $\text{PO}_3\text{R}^4$ ,

$T(\text{CH}_2)_m\text{QR}^4$ ,  $T(\text{CH}_2)_m\text{C}(\text{OR}^5)(\text{H})(\text{CH}_2)_m\text{QR}^4$ ,

wherein  $T$  and  $Q$  are as defined above;

$\text{R}^4$  and  $\text{R}^5$  are each independently selected from the group consisting of hydrogen,  $\text{C}_1$ - $\text{C}_6$  alkyl, substituted alkyl,  $\text{C}_2$ - $\text{C}_6$  alkenyl,  $\text{C}_2$ - $\text{C}_6$  alkynyl,  $\text{N}(\text{C}_1$ - $\text{C}_6$ alkyl)<sub>1</sub> or 2,  $(\text{CH}_2)_n\text{Ar}$ ,  $\text{C}_3$ - $\text{C}_{10}$  cycloalkyl, heterocyclyl, and heteroaryl, or  $\text{R}^4$  and  $\text{R}^5$  together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when  $\text{R}^4$  and  $\text{R}^5$  together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH,  $\text{OR}^4$ ,  $\text{NR}^4\text{R}^5$ ,  $(\text{CH}_2)_m\text{OR}^4$ ,  $(\text{CH}_2)_m\text{NR}^4\text{R}^5$ ,

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T-(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>, CO-T-(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>, NH(CO)T(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>,  
 T-(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>4</sup>, or T(CH<sub>2</sub>)<sub>m</sub>CONR<sup>4</sup>R<sup>5</sup>.

R<sup>6</sup> is alkyl;

R<sup>8</sup> and R<sup>9</sup> independently are H, C<sub>1</sub>-C<sub>3</sub> alkyl, NR<sup>4</sup>R<sup>5</sup>, N(O)R<sup>4</sup>R<sup>5</sup>,

NR<sup>4</sup>R<sup>5</sup>R<sup>6</sup>Y, hydroxy, alkoxy, thiol, thioalkyl, halo, COR<sup>4</sup>,

CO<sub>2</sub>R<sup>4</sup>, CONR<sup>4</sup>R<sup>5</sup>, SO<sub>2</sub>NR<sup>4</sup>R<sup>5</sup>, SO<sub>3</sub>R<sup>4</sup>, PO<sub>3</sub>R<sup>4</sup>, CHO, CN, or

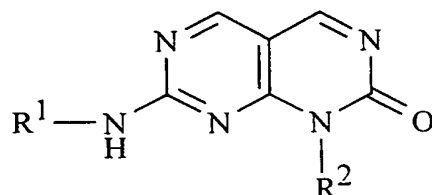
NO<sub>2</sub>;

when the dotted line is absent, R<sup>9</sup> is additionally carbonyl, thiocarbonyl,  
 imine and substituted imine, oxime and oxime ether, and

Y is a halo counter-ion.

2. A compound of Claim 1 wherein Z and G both are N, W is NH, and R<sup>8</sup>,  
 and R<sup>9</sup> both are hydrogen.

3. A compound of Claim 2 having the formula



4. A compound of Claim 3 wherein R<sup>1</sup> is phenyl or substituted phenyl,  
 pyridyl or substituted pyridyl.

5. A compound of Claim 4 wherein R<sup>2</sup> is an alkyl, substituted alkyl, or  
 cycloalkyl unsubstituted or substituted.

6. A compound selected from:

1-Methyl-7-[4-(pyrazol-1-yl)phenylamino]pyrimido[4,5-  
*d*]pyrimidin-2(1*H*)-one;

1-Methyl-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Methyl-7-[4-(4-hydroxypiperidin-1-yl)phenylamino]pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

5 1-Methyl-7-{4-[4-(dimethylamino)piperidin-1-yl]phenylamino}-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Isopropyl-7-[4-(pyrazol-1-yl)phenylamino]pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

10 1-Isopropyl-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Isopropyl-7-[4-(4-hydroxypiperidin-1-yl)phenylamino]pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Isopropyl-7-{4-[4-(dimethylamino)piperidin-1-yl]phenylamino}-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

15 1-Bicyclo[2.2.1]hept-2-yl-7-[4-(pyrazol-1-yl)phenylamino]-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one (exo);

1-Bicyclo[2.2.1]hept-2-yl-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one (exo);

20 1-Bicyclo[2.2.1]hept-2-yl-7-[4-(4-hydroxypiperidin-1-yl)phenylamino]pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one (exo);

1-Bicyclo[2.2.1]hept-2-yl-7-{4-[4-(dimethylamino)piperidin-1-yl]phenylamino}pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one (exo);

7-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-1-cyclopentyl-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

25 7-{4-[4-(2-Amino-4-methyl-pentanoyl)-piperazin-1-yl]-phenylamino}-1-cyclopentyl-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Methyl-7-{4-[4-(3-morpholin-4-ylpropyl)piperidin-1-yl]phenylamino}pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

30 1-Isopropyl-7-{4-[4-(3-morpholin-4-ylpropyl)piperidin-1-yl]phenylamino}pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Cyclopentyl-7-{4-[4-(3-morpholin-4-ylpropyl)piperidin-1-yl]phenylamino}pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

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1-Bicyclo[2.2.1]hept-2-yl-7-{4-[4-(3-morpholin-4-ylpropyl)piperidin-1-yl]phenylamino}pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one (exo);

5 1-Cyclopentyl-7-(4-methanesulfonyl-phenylamino)-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Cyclopentyl-7-(4-fluoro-3-methyl-phenylamino)-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

10 7-[4-(3-Amino-pyrrolidin-1-yl)-phenylamino]-1-cyclopentyl-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

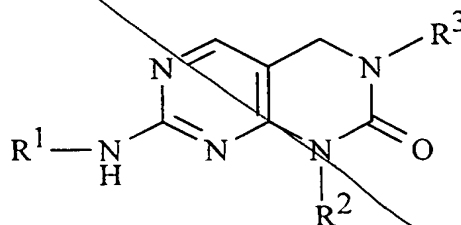
1-Cyclopentyl-7-(4-piperazin-1-yl-phenylamino)-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Cyclopentyl-7-[4-(5-methyl-hexahydro-pyrrolo[3,4-*c*]pyrrol-2-yl)-phenylamino]-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

15 7-[4-(4-Acetyl-piperazin-1-yl)-phenylamino]-1-cycloheptyl-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one; and

1-Cyclopentyl-7-(pyridin-4-ylamino)pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one.

7. A compound of Claim 2 having the formula



20 8. A compound of Claim 7 wherein R<sup>1</sup> is alkyl, pyridyl, or phenyl, each optionally substituted with hydroxy, alkoxy, NR<sup>4</sup>R<sup>5</sup>, or T(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>.

9. A compound selected from:

1-Methyl-7-[4-(pyrazol-1-yl)phenylamino]-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

25 1-Methyl-7-[4-(4-methylpiperazin-1-yl)phenylamino]-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

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7-{4-[4-(2-Amino-4-methyl-pentanoyl)-piperazin-1-yl]-phenylamino}-1-cyclopentyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Methyl-7-{4-[4-(3-morpholin-4-ylpropyl)piperidin-1-yl]phenylamino}-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Isopropyl-7-{4-[4-(3-morpholin-4-ylpropyl)piperidin-1-yl]phenylamino}-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

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1-Cyclopentyl-7-{4-[4-(3-morpholin-4-ylpropyl)piperidin-1-yl]phenylamino}-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

yl]phenylamino}-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Bicyclo[2.2.1]hept-2-yl-7-{4-[4-(3-morpholin-4-ylpropyl)piperidin-1-yl]phenylamino}-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one (exo);

5 1-Cyclopentyl-7-(pyridin-4-ylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Cyclopentyl-7-(4-methanesulfonyl-phenylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Cyclopentyl-7-(4-fluoro-3-methyl-phenylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

10 7-[4-(3-Amino-pyrrolidin-1-yl)-phenylamino]-1-cyclopentyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-[4-(4-Acetyl-piperazin-1-yl)-phenylamino]-1-cyclopentyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

15 1-Cyclopentyl-7-(4-piperazin-1-yl-phenylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

1-Cyclopentyl-7-[4-(5-methyl-hexahydro-pyrrolo[3,4-*c*]pyrrol-2-yl)-phenylamino]-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

20 7-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-3-(3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-3-(2-chloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

25 7-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-3-(2,6-dichloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-3-(2-methyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

30 7-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-3-(2,6-dimethyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

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7-[4-(2-Diethylamino-ethoxy)-phenylamino]-3-(3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-[4-(2-Diethylamino-ethoxy)-phenylamino]-3-(2-chloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-[4-(2-Diethylamino-ethoxy)-phenylamino]-3-(2,6-dichloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-[4-(2-Diethylamino-ethoxy)-phenylamino]-3-(2-methyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-[4-(2-Diethylamino-ethoxy)-phenylamino]-3-(2,6-dimethyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-(4-Diethylamino-butylamino)-3-(3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-(4-Diethylamino-butylamino)-3-(2-chloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-(4-Diethylamino-butylamino)-3-(2,6-dichloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-(4-Diethylamino-butylamino)-3-(2-methyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-(4-Diethylamino-butylamino)-3-(2,6-dimethyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-(Pyridin-4-ylamino)-3-(3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-(Pyridin-4-ylamino)-3-(2-chloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-(Pyridin-4-ylamino)-3-(2,6-dichloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-(Pyridin-4-ylamino)-3-(2,6-dimethyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;



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7-(Pyridin-4-ylamino)-3-(2-methyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-(Pyridin-4-ylamino)-3-(2,6-dichloro-3,5-dimethoxy-phenyl)-1-cyclopentyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

5 3-(2-Chloro-3,5-dimethoxy-phenyl)-7-(4-diethylamino-butylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

3-(2-Chloro-3,5-dimethoxy-phenyl)-7-[4-(2-diethylamino-ethoxy)-phenylamino]-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

10 3-(2-Chloro-3,5-dimethoxy-phenyl)-7-(pyridin-4-ylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

3-(3,5-Dimethoxy-phenyl)-7-(pyridin-4-ylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

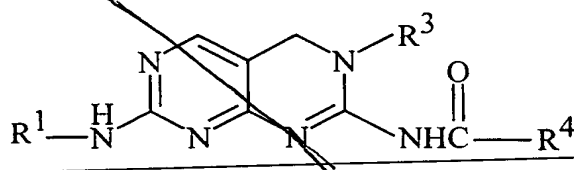
7-[4-(2-Diethylamino-ethoxy)-phenylamino]-3-(3,5-dimethoxy-phenyl)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

15 3-(2,6-Dichloro-3,5-dimethoxy-phenyl)-7-(pyridin-4-ylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one; and

3-(2,6-Dichloro-3,5-dimethoxy-phenyl)-7-[4-(2-diethylamino-ethoxy)-phenylamino]-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one.

Sub 10. A compound of Claim 2 having the formula  
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11. A compound selected from:

1-[7-[4-(2-Diethylamino-ethoxy)-phenylamino]-3-(3,5-dimethoxy-phenyl)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl]-3-ethyl-urea;

25 1-{3-(2-Chloro-3,5-dimethoxy-phenyl)-7-[4-(2-diethylamino-ethoxy)-phenylamino]-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl}-3-ethyl-urea;

1-*tert*-Butyl-3-[7-[4-(2-diethylamino-ethoxy)-phenylamino]-3-(3,5-dimethoxy-phenyl)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl]-urea;

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1-*tert*-Butyl-3-{3-(2-chloro-3,5-dimethoxy-phenyl)-7-[4-(2-diethylamino-ethoxy)-phenylamino]-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl}-urea;

5 1-*tert*-Butyl-3-[3-(3,5-dimethoxy-phenyl)-7-(pyridin-4-ylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl]-urea;

1-[3-(3,5-Dimethoxy-phenyl)-7-(pyridin-4-ylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl]-3-ethyl-urea;

1-*tert*-Butyl-3-[3-(2-chloro-3,5-dimethoxy-phenyl)-7-(pyridin-4-ylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl]-urea;

10 1-[3-(2-Chloro-3,5-dimethoxy-phenyl)-7-(pyridin-4-ylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl]-3-ethyl-urea;

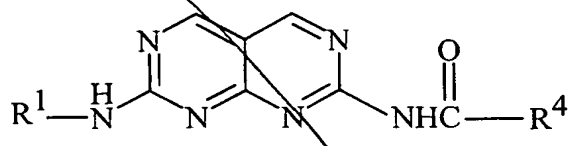
1-[3-(2-Chloro-3,5-dimethoxy-phenyl)-7-(4-diethylamino-butylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl]-3-ethyl-urea;

15 3-Methyl-N-{7-[4-(5-methyl-hexahydro-pyrrolo[3,4-*c*]pyrrol-2-yl)-phenylamino]-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl}-butyramide;

1-{7-[4-(4-Acetyl-piperazin-1-yl)-phenylamino]-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl}-3-isopropyl-urea; and

20 1-*tert*-Butyl-3-[3-(2-chloro-3,5-dimethoxy-phenyl)-7-(4-diethylamino-butylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2-yl]-urea.

12. A compound of Claim 2 having the formula



13. A compound selected from:

25 1-[7-(4-Fluoro-phenylamino)-pyrimido[4,5-*d*]pyrimidin-2-yl]-3-methyl-urea;

1-Isopropyl-3-(7-phenylamino-pyrimido[4,5-*d*]pyrimidin-2-yl)-urea;

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1-{7-[4-(3-Aminomethyl-pyrrolidin-1-yl)-phenylamino]-pyrimido[4,5-*d*]pyrimidin-2-yl}-3-isopropyl-urea;

1-Isopropyl-3-[7-(4-piperazin-1-yl-phenylamino)-pyrimido[4,5-*d*]pyrimidin-2-yl]-urea;

5 1-{7-[4-(4-Acetyl-piperazin-1-yl)-phenylamino]-pyrimido[4,5-*d*]pyrimidin-2-yl}-3-isopropyl-urea;

N-{7-[4-(3-Amino-pyrrolidin-1-yl)-phenylamino]-pyrimido[4,5-*d*]pyrimidin-2-yl}-3-methyl-butylamide;

10 N-[7-(4-Piperazin-1-yl-phenylamino)-pyrimido[4,5-*d*]pyrimidin-2-yl]-isobutylamide;

N-{7-[4-(4-Acetyl-piperazin-1-yl)-phenylamino]-pyrimido[4,5-*d*]pyrimidin-2-yl}-3-methyl-butylamide;

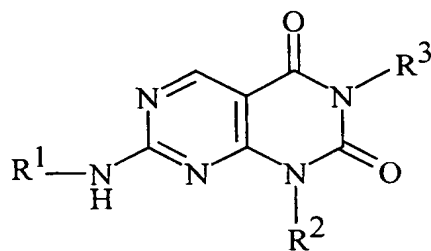
3-Methyl-N-[7-(pyridin-4-ylamino)-pyrimido[4,5-*d*]pyrimidin-2-yl]-butylamide;

15 1-Isopropyl-3-[7-(pyridin-4-ylamino)-pyrimido[4,5-*d*]pyrimidin-2-yl]-urea; and

N-{7-[4-(3-Aminomethyl-pyrrolidin-1-yl)-phenylamino]-pyrimido[4,5-*d*]pyrimidin-2-yl}-3-methyl-butylamide.

14. A compound of Claim 1 wherein W is S, SO, or SO<sub>2</sub>.

20 15. A compound of Claim 1 having the formula



16. A compound selected from:

1-Isopropyl-7-[4-(4-methylpiperazin-1-yl)phenylamino]-1*H*-pyrimido[4,5-*d*]pyrimidine-2,4-dione;

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7-[4-(2-Diethylaminoethoxy)phenylamino]-1-isopropyl-1*H*-pyrimido[4,5-*d*]pyrimidine-2,4-dione;

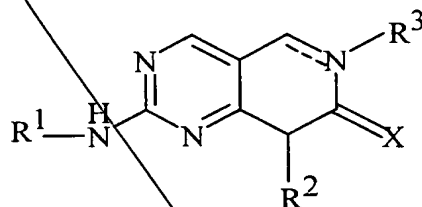
7-(4-Diethylamino-butylamino)-3-(3,5-dimethoxy-phenyl)-1-ethyl-1*H*-pyrimido[4,5-*d*]pyrimidine-2,4-dione;

5 7-[4-(2-Diethylamino-ethoxy)-phenylamino]-3-(3,5-dimethoxy-phenyl)-1-ethyl-1*H*-pyrimido[4,5-*d*]pyrimidine-2,4-dione; and

7-(Pyridin-4-ylamino)-3-(3,5-dimethoxy-phenyl)-1-ethyl-1*H*-pyrimido[4,5-*d*]pyrimidine-2,4-dione.

10 17. A compound of Claim 1 wherein Z is N, G is CH, W is NH, and R<sup>8</sup> and R<sup>9</sup> both are hydrogen.

18. A compound of Claim 17 having the formula



15 19. A compound selected from:

2-[4-(3-Amino-pyrrolidin-1-yl)-phenylamino]-8-isopropyl-8*H*-pyrido[4,3-*d*]pyrimidin-7-one;

8-Cyclopentyl-2-[4-(hexahydro-pyrrolo[3,4-*c*]pyrrol-2-yl)-phenylamino]-8*H*-pyrido[4,3-*d*]pyrimidin-7-one;

2-[4-(4-Acetyl-piperazin-1-yl)-phenylamino]-8-cyclopentyl-8*H*-pyrido[4,3-*d*]pyrimidin-7-one;

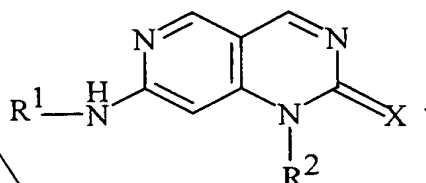
20 N-{2-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-8-cyclopentyl-pyrido[4,3-*d*]pyrimidin-7-yl}-2,2-dimethyl-propionamide; and

N-(2-{4-[4-(2-Amino-4-methyl-pentanoyl)-piperazin-1-yl]-phenylamino}-8-cyclopentyl-pyrido[4,3-*d*]pyrimidin-7-yl)-2,2-dimethyl-propionamide.

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20. A compound of Claim 1 wherein Z is CH, G is N, W is NH, and R<sup>8</sup> and R<sup>9</sup> both are hydrogen.

21. A compound of Claim 20 having the formula



22. A compound selected from:

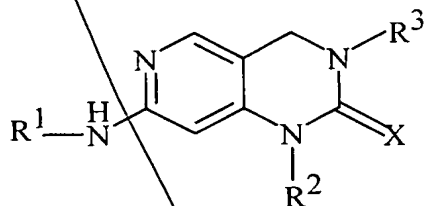
- 1-(2-Benzyloxyethyl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;  
 1-(Thiophen-2-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;  
 1-(Thiophen-2-ylmethyl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;  
 1-(Tetrahydrofuran-2-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;  
 1-(Hexa-2,4-diene-1-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;  
 1-(Prop-2-yne-1-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;  
 1-[3-(Dimethylamino)prop-1-yl]-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;  
 1-(3-Hydroxyprop-1-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;  
 1-(Pyridin-4-ylmethyl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;  
 1-(3,5-Dimethylhept-1-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

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1-Cyclopentyl-7-(4-piperazin-1-ylphenylamino)pyrido[4,3-*d*]pyrimidin-2(1*H*)-one; and

7-[4-(3-Aminopyrrolidin-1-yl)phenylamino]-1-cyclopentylpyrido[4,3-*d*]pyrimidin-2(1*H*)-one.

- 5 23. A compound of Claim 20 having the formula



24. A compound selected from:

1-(2-Benzoyloxyethyl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

10 1-(Thiophen-2-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

1-(Thiophen-2-ylmethyl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

15 1-(Tetrahydrofuran-2-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

1-(Hexa-2,4-diene-1-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

1-(Prop-2-yne-1-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

20 1-[3-(Dimethylamino)prop-1-yl]-7-[4-(4-methylpiperazin-1-yl)phenylamino]-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

1-(3-Hydroxyprop-1-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

25 1-(Pyridin-4-ylmethyl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

1-(3,5-Dimethylhept-1-yl)-7-[4-(4-methylpiperazin-1-yl)phenylamino]-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

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3-(3,5-Dimethoxy-phenyl)-7-(pyridin-4-ylamino)-1-ethyl-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

3-(2-Chloro-3,5-Dimethoxy-phenyl)-7-(pyridin-4-ylamino)-1-ethyl-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

5 3-(2,6-Dichloro-3,5-Dimethoxy-phenyl)-7-(pyridin-4-ylamino)-1-ethyl-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

3-(2-Methyl-3,5-Dimethoxy-phenyl)-7-(pyridin-4-ylamino)-1-ethyl-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

10 3-(2,6-Dimethyl-3,5-Dimethoxy-phenyl)-7-(pyridin-4-ylamino)-1-ethyl-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

7-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-3-(3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

15 7-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-3-(2-chloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

7-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-3-(2,6-dichloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one;

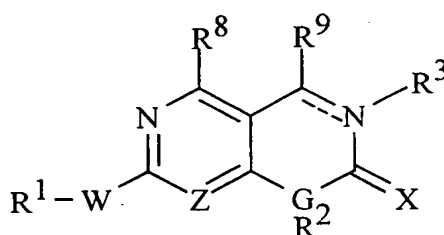
20 7-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-3-(2-methyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one; and

25 7-[4-(4-Aminoacetyl-piperazin-1-yl)-phenylamino]-3-(2,6-dimethyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrido[4,3-*d*]pyrimidin-2(1*H*)-one.

25. A method for controlling proliferative disorders selected from the group consisting of cancer, psoriasis, vascular smooth muscle proliferation associated with a disorder selected from the group consisting of atherosclerosis, postsurgical vascular stenosis, and restenosis in mammals, diabetic retinopathy and angiogenesis, comprising administering to said mammal a therapeutically effective amount of a compound of Formula I

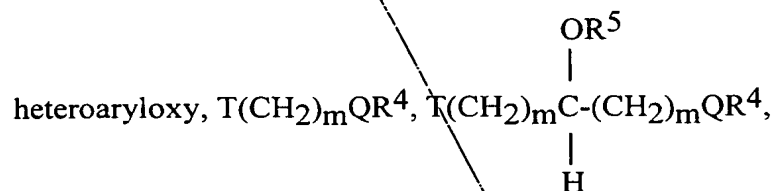
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I

$R^1$ ,  $R^2$ , and  $R^{10}$  are independently selected from the group consisting of  
 H,  $(CH_2)_nAr$ ,  $COR^4$ ,  $(CH_2)_n$ heteroaryl,  $(CH_2)_n$ heterocyclyl,  
 C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, and C<sub>2</sub>-C<sub>10</sub>  
 alkynyl, wherein n is 0, 1, 2, or 3, and the  $(CH_2)_nAr$ ,  
 $(CH_2)_n$ heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups  
 are optionally substituted by up to 5 groups selected from  $NR^4R^5$ ,  
 $N(O)R^4R^5$ ,  $NR^4R^5R^6Y$ , alkyl, phenyl, substituted phenyl,  
 $(CH_2)_n$ heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo,  
 $COR^4$ ,  $CO_2R^4$ ,  $CONR^4R^5$ ,  $SO_2NR^4R^5$ ,  $SO_3R^4$ ,  $PO_3R^4$ ,  
 aldehyde, nitrile, nitro,



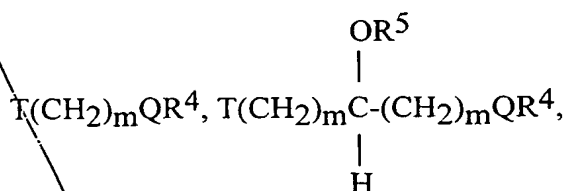
$C(O)T(CH_2)_mQR^4$ ,  $NHC(O)T(CH_2)_mQR^4$ ,  
 $T(CH_2)_mC(O)NR^4NR^5$ , or  $T(CH_2)_mCO_2R^4$  wherein each m is  
 independently 1-6, T is O, S,  $NR^4$ ,  $N(O)R^4$ ,  $NR^4R^6Y$ , or  $CR^4R^5$ ,  
 and Q is O, S,  $NR^5$ ,  $N(O)R^5$ , or  $NR^5R^6Y$ ;

when the dotted line is present,  $R^3$  is absent;

otherwise  $R^3$  has the meanings of  $R^2$ , wherein  $R^2$  is as defined above, as  
 well as OH,  $NR^4R^5$ ,  $COOR^4$ ,  $OR^4$ ,  $CONR^4R^5$ ,  $SO_2NR^4R^5$ ,  
 $SO_3R^4$ ,  $PO_3R^4$ ,



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wherein T and Q are as defined above;

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$\text{R}^4$  and  $\text{R}^5$  are each independently selected from the group consisting of hydrogen,  $\text{C}_1$ - $\text{C}_6$  alkyl, substituted alkyl,  $\text{C}_2$ - $\text{C}_6$  alkenyl,  $\text{C}_2$ - $\text{C}_6$  alkynyl,  $\text{N}(\text{C}_1\text{-C}_6\text{alkyl})_1$  or 2,  $(\text{CH}_2)_n\text{Ar}$ ,  $\text{C}_3$ - $\text{C}_{10}$  cycloalkyl, heterocyclyl, and heteroaryl, or  $\text{R}^4$  and  $\text{R}^5$  together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

15

when  $\text{R}^4$  and  $\text{R}^5$  together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH,  $\text{OR}^4$ ,  $\text{NR}^4\text{R}^5$ ,  $(\text{CH}_2)_m\text{OR}^4$ ,  $(\text{CH}_2)_m\text{NR}^4\text{R}^5$ ,  $\text{T}-(\text{CH}_2)_m\text{QR}^4$ ,  $\text{CO-T}-(\text{CH}_2)_m\text{QR}^4$ ,  $\text{NH}(\text{CO})\text{T}-(\text{CH}_2)_m\text{QR}^4$ ,  $\text{T}-(\text{CH}_2)_m\text{CO}_2\text{R}^4$ , or  $\text{T}-(\text{CH}_2)_m\text{CONR}^4\text{R}^5$ .

20

$\text{R}^6$  is alkyl;

$\text{R}^8$  and  $\text{R}^9$  independently are H,  $\text{C}_1$ - $\text{C}_3$  alkyl,  $\text{NR}^4\text{R}^5$ ,  $\text{N}(\text{O})\text{R}^4\text{R}^5$ ,  $\text{NR}^4\text{R}^5\text{R}^6\text{Y}$ , hydroxy, alkoxy, thiol, thioalkyl, halo,  $\text{COR}^4$ ,  $\text{CO}_2\text{R}^4$ ,  $\text{CONR}^4\text{R}^5$ ,  $\text{SO}_2\text{NR}^4\text{R}^5$ ,  $\text{SO}_3\text{R}^4$ ,  $\text{PO}_3\text{R}^4$ , CHO, CN, or  $\text{NO}_2$ ;

25

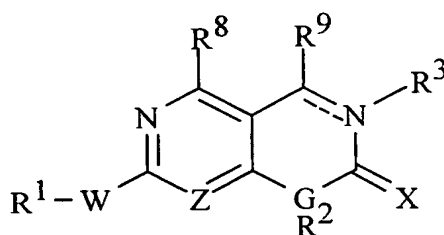
when the dotted line is absent,  $\text{R}^9$  is additionally carbonyl, thiocarbonyl, imine and substituted imine, oxime and oxime ether, and Y is a halo counter-ion.

26. A method of inhibiting a cyclin-dependent kinase comprising contacting the cyclin-dependent kinase with a compound of Formula I

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I

$R^1$ ,  $R^2$ , and  $R^{10}$  are independently selected from the group consisting of H,  $(CH_2)_nAr$ ,  $COR^4$ ,  $(CH_2)_n$ heteroaryl,  $(CH_2)_n$ heterocyclyl,  $C_1$ - $C_{10}$  alkyl,  $C_3$ - $C_{10}$  cycloalkyl,  $C_2$ - $C_{10}$  alkenyl, and  $C_2$ - $C_{10}$  alkynyl, wherein n is 0, 1, 2, or 3, and the  $(CH_2)_nAr$ ,  $(CH_2)_n$ heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from  $NR^4R^5$ ,  $N(O)R^4R^5$ ,  $NR^4R^5R^6Y$ , alkyl, phenyl, substituted phenyl,  $(CH_2)_n$ heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo,  $COR^4$ ,  $CO_2R^4$ ,  $CONR^4R^5$ ,  $SO_2NR^4R^5$ ,  $SO_3R^4$ ,  $PO_3R^4$ , aldehyde, nitrile, nitro,

heteroaryloxy, T(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>, T(CH<sub>2</sub>)<sub>m</sub>C(OR<sup>5</sup>)(H)-(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>,

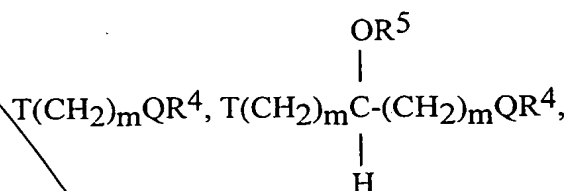
$$\text{C(O)T(CH}_2)_m\text{QR}^4, \text{NHC(O)T(CH}_2)_m\text{QR}^4,$$

~~T(CH<sub>2</sub>)<sub>m</sub>C(O)NR<sup>4</sup>NR<sup>5</sup>, or T(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>4</sup> wherein each m is independently 1-6, T is O, S, NR<sup>4</sup>, N(O)R<sup>4</sup>, NR<sup>4</sup>R<sup>6</sup>Y, or CR<sup>4</sup>R<sup>5</sup>, and Q is O, S, NR<sup>5</sup>, N(O)R<sup>5</sup>, or NR<sup>5</sup>R<sup>6</sup>Y;~~

when the dotted line is present,  $R^3$  is absent;

otherwise R<sup>3</sup> has the meanings of R<sup>2</sup>, wherein R<sup>2</sup> is as defined above, as well as OH, NR<sup>4</sup>R<sup>5</sup>, COOR<sup>4</sup>, OR<sup>4</sup>, CONR<sup>4</sup>R<sup>5</sup>, SO<sub>2</sub>NR<sup>4</sup>R<sup>5</sup>, SO<sub>3</sub>R<sup>4</sup>, PO<sub>3</sub>R<sup>4</sup>,

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wherein T and Q are as defined above;

R<sup>4</sup> and R<sup>5</sup> are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, substituted alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, N(C<sub>1</sub>-C<sub>6</sub>alkyl)<sub>1</sub> or 2, (CH<sub>2</sub>)<sub>n</sub>Ar, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, heterocyclyl, and heteroaryl, or R<sup>4</sup> and R<sup>5</sup> together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

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when R<sup>4</sup> and R<sup>5</sup> together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR<sup>4</sup>, NR<sup>4</sup>R<sup>5</sup>, (CH<sub>2</sub>)<sub>m</sub>OR<sup>4</sup>, (CH<sub>2</sub>)<sub>m</sub>NR<sup>4</sup>R<sup>5</sup>, T-(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>, CO-T-(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>, NH(CO)T(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>, T-(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>4</sup>, or T(CH<sub>2</sub>)<sub>m</sub>CONR<sup>4</sup>R<sup>5</sup>.

20

R<sup>6</sup> is alkyl;

R<sup>8</sup> and R<sup>9</sup> independently are H, C<sub>1</sub>-C<sub>3</sub> alkyl, NR<sup>4</sup>R<sup>5</sup>, N(O)R<sup>4</sup>R<sup>5</sup>, NR<sup>4</sup>R<sup>5</sup>R<sup>6</sup>Y, hydroxy, alkoxy, thiol, thioalkyl, halo, COR<sup>4</sup>, CO<sub>2</sub>R<sup>4</sup>, CONR<sup>4</sup>R<sup>5</sup>, SO<sub>2</sub>NR<sup>4</sup>R<sup>5</sup>, SO<sub>3</sub>R<sup>4</sup>, PO<sub>3</sub>R<sup>4</sup>, CHO, CN, or NO<sub>2</sub>;

25

when the dotted line is absent, R<sup>9</sup> is additionally carbonyl, thiocarbonyl, imine and substituted imine, oxime and oxime ether, and Y is a halo counter-ion.

27. A method of Claim 26 wherein said cyclin-dependent kinase is cdc2.

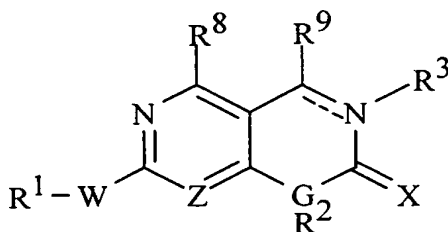
28. A method of Claim 26 wherein said cyclin-dependent kinase is cdk2.

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29. A method of Claim 26 wherein said cyclin-dependent kinase is cdk4 or cdk6.

30. A method of inhibiting a growth factor-mediated tyrosine kinase comprising contacting said growth factor-mediated kinase with a compound of Formula I



I

and the pharmaceutically acceptable salts thereof,  
wherein:

the dotted line represents an optional double bond;

Z is N or CH;

G is N or CH;

W is NH, S, SO, or SO<sub>2</sub>;

X is either O, S, or NR<sup>10</sup>;

R<sup>1</sup>, R<sup>2</sup>, and R<sup>10</sup> are independently selected from the group consisting of

H, (CH<sub>2</sub>)<sub>n</sub>Ar, COR<sup>4</sup>, (CH<sub>2</sub>)<sub>n</sub>heteroaryl, (CH<sub>2</sub>)<sub>n</sub>heterocyclyl,

C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, and C<sub>2</sub>-C<sub>10</sub>

alkynyl, wherein n is 0, 1, 2, or 3, and the (CH<sub>2</sub>)<sub>n</sub>Ar,

(CH<sub>2</sub>)<sub>n</sub>heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups

are optionally substituted by up to 5 groups selected from NR<sup>4</sup>R<sup>5</sup>,

N(O)R<sup>4</sup>R<sup>5</sup>, NR<sup>4</sup>R<sup>5</sup>R<sup>6</sup>Y, alkyl, phenyl, substituted phenyl,

(CH<sub>2</sub>)<sub>n</sub>heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo,

COR<sup>4</sup>, CO<sub>2</sub>R<sup>4</sup>, CONR<sup>4</sup>R<sup>5</sup>, SO<sub>2</sub>NR<sup>4</sup>R<sup>5</sup>, SO<sub>3</sub>R<sup>4</sup>, PO<sub>3</sub>R<sup>4</sup>,

aldehyde, nitrile, nitro,

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$T-(CH_2)_mQR^4$ ,  $CO-T-(CH_2)_mQR^4$ ,  $NH(CO)T(CH_2)_mQR^4$ ,  
 $T-(CH_2)_mCO_2R^4$ , or  $T(CH_2)_mCONR^4R^5$ .

$R^6$  is alkyl;

$R^8$  and  $R^9$  independently are H,  $C_1$ - $C_3$  alkyl,  $NR^4R^5$ ,  $N(O)R^4R^5$ ,  
 $NR^4R^5R^6Y$ , hydroxy, alkoxy, thiol, thioalkyl, halo,  $COR^4$ ,  
 $CO_2R^4$ ,  $CONR^4R^5$ ,  $SO_2NR^4R^5$ ,  $SO_3R^4$ ,  $PO_3R^4$ , CHO, CN, or  
 $NO_2$ ;

when the dotted line is absent,  $R^9$  is additionally carbonyl, thiocarbonyl,  
imine and substituted imine, oxime and oxime ether, and

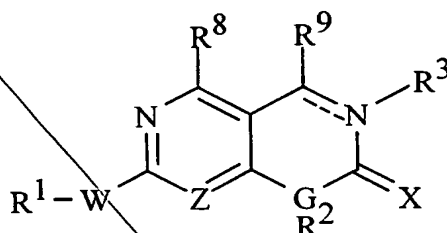
Y is a halo counter-ion.

31. A method of Claim 30 wherein said growth factor-mediated tyrosine  
kinase is platelet derived growth factor (PDGF).

32. A method of Claim 30 wherein said growth factor-mediated tyrosine  
kinase is fibroblast growth factor (FGF).

33. A method of Claim 30 wherein said growth factor-mediated tyrosine  
kinase is vascular endothelial growth factor (VEGF).

34. A method of inhibiting a non-receptor tyrosine kinase comprising  
contacting said non-receptor tyrosine kinase with a compound of  
Formula I



and the pharmaceutically acceptable salts thereof,  
wherein:

the dotted line represents an optional double bond;

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$Z$  is N or CH;

~~G is N or CH;~~

W is ~~NH~~, S, SO, or SO<sub>2</sub>;

X is either O, S, or NR<sup>10</sup>;

$R^1, R^2$ , and  $R^{10}$  are independently selected from the group consisting of

H, (CH<sub>2</sub>)<sub>n</sub>Ar, COR<sup>4</sup>, (CH<sub>2</sub>)<sub>n</sub>heteroaryl, (CH<sub>2</sub>)<sub>n</sub>heterocyclyl,

C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, and C<sub>2</sub>-C<sub>10</sub>

alkynyl, wherein n is 0, 1, 2, or 3, and the  $(\text{CH}_2)_n\text{Ar}$ ,

(CH<sub>2</sub>)<sub>n</sub>heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups

are optionally substituted by up to 5 groups selected from  $\text{NR}^4\text{R}^5$ ,

N(O)R<sup>4</sup>R<sup>5</sup>, NR<sup>4</sup>~~R<sup>5</sup>~~R<sup>6</sup>Y, alkyl, phenyl, substituted phenyl,

(CH<sub>2</sub>)<sub>n</sub>heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo,

$\text{COR}^4, \text{CO}_2\text{R}^4, \text{CONR}^4\text{R}^5, \text{SO}_2\text{NR}^4\text{R}^5, \text{SO}_3\text{R}^4, \text{PO}_3\text{R}^4,$

aldehyde, nitrile, nitro,

heteroaryloxy, T(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>, T(CH<sub>2</sub>)<sub>m</sub>C(OR<sup>5</sup>)(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>,  
|  
H

$$\text{C(O)T(CH}_2)_m\text{QR}^4, \text{NHC(O)T(CH}_2)_m\text{QR}^4,$$

$\text{T}(\text{CH}_2)_m\text{C}(\text{O})\text{NR}^4\text{NR}^5$ , or  $\text{T}(\text{CH}_2)_m\text{CO}_2\text{R}^4$  wherein each  $m$  is

independently 1-6, T is O, S,  $\text{NR}^4$ ,  $\text{N}(\text{O})\text{R}^4$ ,  $\text{NR}^4\text{R}^6\text{Y}$ , or  $\text{CR}^4\text{R}^5$ ,

and Q is O, S, NR<sup>5</sup>, N(O)R<sup>5</sup>, or NR<sup>5</sup>R<sup>6</sup>Y;

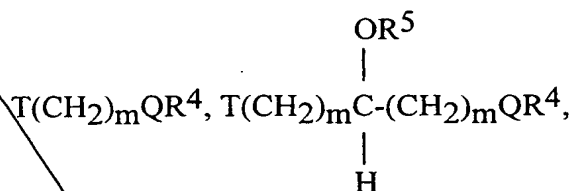
when the dotted line is present,  $R^3$  is absent;

otherwise  $R^3$  has the meanings of  $R^2$ , wherein  $R^2$  is as defined above, as

well as OH, NR<sup>4</sup>R<sup>5</sup>, COOR<sup>4</sup>, OR<sup>4</sup>, CONR<sup>4</sup>R<sup>5</sup>, SO<sub>2</sub>NR<sup>4</sup>R<sup>5</sup>,

 $\text{SO}_3\text{R}^4, \text{PO}_3\text{R}^4,$

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wherein T and Q are as defined above;

R<sup>4</sup> and R<sup>5</sup> are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, substituted alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, N(C<sub>1</sub>-C<sub>6</sub>alkyl)<sub>1</sub> or 2, (CH<sub>2</sub>)<sub>n</sub>Ar, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, heterocyclyl, and heteroaryl, or R<sup>4</sup> and R<sup>5</sup> together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R<sup>4</sup> and R<sup>5</sup> together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR<sup>4</sup>, NR<sup>4</sup>R<sup>5</sup>, (CH<sub>2</sub>)<sub>m</sub>OR<sup>4</sup>, (CH<sub>2</sub>)<sub>m</sub>NR<sup>4</sup>R<sup>5</sup>, T-(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>, CO-T-(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>, NH(CO)T(CH<sub>2</sub>)<sub>m</sub>QR<sup>4</sup>, T-(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>4</sup>, or T(CH<sub>2</sub>)<sub>m</sub>CONR<sup>4</sup>R<sup>5</sup>.

R<sup>6</sup> is alkyl;

R<sup>8</sup> and R<sup>9</sup> independently are H, C<sub>1</sub>-C<sub>3</sub> alkyl, NR<sup>4</sup>R<sup>5</sup>, N(O)R<sup>4</sup>R<sup>5</sup>, NR<sup>4</sup>R<sup>5</sup>R<sup>6</sup>Y, hydroxy, alkoxy, thiol, thioalkyl, halo, COR<sup>4</sup>, CO<sub>2</sub>R<sup>4</sup>, CONR<sup>4</sup>R<sup>5</sup>, SO<sub>2</sub>NR<sup>4</sup>R<sup>5</sup>, SO<sub>3</sub>R<sup>4</sup>, PO<sub>3</sub>R<sup>4</sup>, CHO, CN, or NO<sub>2</sub>;

when the dotted line is absent, R<sup>9</sup> is additionally carbonyl, thiocarbonyl, imine and substituted imine, oxime and oxime ether, and Y is a halo counter-ion.

35. A method of Claim 33 wherein said non-receptor tyrosine kinase is selected from a transforming gene of the Rous sarcoma retrovirus (Src) family.



36. A method of inhibiting a serine kinase in a mammal comprising administering a serine kinase inhibiting amount of a compound of Claim 1.

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37. A method of treating a subject suffering from diseases caused by vascular smooth muscle cell proliferation comprising administering to said subject a therapeutically effective amount of a compound of Claim 1.

38. A method of treating a subject suffering from cancer comprising administering to said subject a therapeutically effective amount of a compound of Claim 1.

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39. A method of inhibiting angiogenesis in a mammal comprising administering an anti-angiogenic effective amount of a compound of Claim 1.

40. A method according to Claim 39 wherein the disease state caused by angiogenesis is selected from human cancer, macular degeneration, diabetic retinopathy, surgical adhesions, and psoriasis.

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41. A method of inhibiting a wee-1 kinase enzyme in a mammal comprising administering a wee-1 kinase inhibiting amount of a compound of Claim 1.

42. A compound selected from:

7-[3-(Carboxy)-phenylamino]-3-(2,6-dichloro-phenyl)-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

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7-[3-(N-Dimethylaminopropyl-carboxamide)-phenylamino]-3-(2,6-dichloro-phenyl)-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

25

7-[3-(N-Dimethylaminopropyl-carboxamide)-phenylamino]-3-(2,6-dichloro-3-hydroxy-phenyl)-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-[3-(Carboxy)-phenylamino]-3-(2,6-dichloro-3-hydroxy-phenyl)-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

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3-(2,6-Dichloro-phenyl)-7-[4-(2-ethylamino-ethoxy)-phenylamino]-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

3-(2,6-Dichloro-3-hydroxy-phenyl)-7-[4-(2-ethylamino-ethoxy)-phenylamino]-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

5 7-[4-(Carboxamide)-phenylamino]-3-(2,6-dichloro-phenyl)-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-[4-(Carboxamide)-phenylamino]-3-(2,6-dichloro-3-hydroxy-phenyl)-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

10 3-(2,6-Dichloro-phenyl)-7-(3-hydroxymethyl-phenylamino)-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

3-(2,6-Dichloro-phenyl)-7-(4-morpholin-4-yl-phenylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

3-(2,6-Dichloro-3-hydroxy-phenyl)-1-methyl-7-(4-morpholin-4-yl-phenylamino)-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

15 3-(2,6-Dichloro-3-hydroxy-phenyl)-7-(3-hydroxymethyl-phenylamino)-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

7-[4-(3-Carboxypropyl)-phenylamino]-3-(2,6-dichloro-phenyl)-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

20 7-[4-(3-Carboxypropyl)-phenylamino]-3-(2,6-dichloro-3-hydroxy-phenyl)-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one;

3-(2,6-Dichloro-phenyl)-7-[4-(formyl-phenylamino)]-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one; and

3-(2,6-Dichloro-3-hydroxy-phenyl)-7-[4-(formyl-phenylamino)]-1-methyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidin-2(1*H*)-one.

- 25 43. A pharmaceutical formulation comprising a compound of Claim 1 in combination with a pharmaceutically acceptable carrier, diluent, or excipient.

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